AMENDMENTS TO THE SPECIFICATION

Please replace the fourth paragraph on page 37 of the specification with the following amended paragraph:

Figures 2 and 3 ~~Figure 2~~. Histologic scoring of synovial inflammation and fibrin staining in rheumatoid arthritis (RA) and osteoarthritis (OA) synovial tissues. Specimens were graded separately for inflammation, using a composite score that evaluates synovial lining hyperplasia, lymphocytic infiltration, and sublining layer hyperplasia (0-3 scale for each component; maximum score = 9) and fibrin deposition (0-3 scale). The horizontal bars represent the median scores. Differences between groups were analyzed with Fisher's exact test, * = $P < 0.003$.

Please replace the paragraph bridging pages 37-38 of the specification with the following amended paragraph:

Figures 4 and 5 ~~Figure 3~~. Tissue factor (TF) and TF pathway inhibitor (TFPI) measurements in tissue extracts prepared from rheumatoid arthritis (RA) and ostcoarthritis (OA) synovial specimens. TF (a) and TFPI activities (b) were measured using chromogenic assays adjusted for protein concentration of the tissue attract, and were expressed as arbitrary units (AU) per milligram of protein (prot). TF antigenic (Ag) activity was determined by enzyme linked immunosorbent assay (c), and TF mRNA was determined by RNase protection assay and was expressed as AU after normalization with GAPDH mRNA levels (d). Results are expressed as the mean ± SEM. Differences between groups were analyzed by Wilcoxon's rank sum test. * = $P < 0.02$ (n) and $P < 0.05$ (b).

Please replace the first full paragraph on page 38 of the specification with the following amended paragraph:

Figure 6 ~~Figure 4~~. Relationship between tissue factor (TF) and TF pathway inhibitor (TFPI) activity. For TF expression there was a close correlation between the amount of TF mRNA and the corresponding protein. In contrast, no correlation existed between ~~TFactivity~~ TF activity and TF antigenic (Ag) levels (b) or between TF activity and TF mRNA levels (c). A strong negative correlation between TF activity and TFPI activity was evident (d). The strength of the relationship ~~relattionship~~ between variables was assessed by Spearman's correlation test, a.u. = arbitrary units.

Please replace the second full paragraph on page 38 of the specification with the following amended paragraph:

Figure 7 ~~Figure 5~~. Associations between tissue factor (TF) activity. TF pathway inhibitor (TFPI) activity, and histologic scores. Among all patients, TF activity was significantly associated with the synovial fibrin score (a) and the inflammation score (b). Conversely, TFPI activity was negatively associated with the fibrin score (c) Associations were determined ~~deteemined~~ by Fisher's exact test. (a.u. = arbitrary units).

Please replace the third full paragraph on page 38 of the specification with the following amended paragraph:

Figure 8 ~~Figure 6~~. Clinical and histological features of the knee joints and coagulation times for control mice and mice with antigen induces arthritis (AIA) treated with active site blocked factor VII (FVIIai). The time course of knee joint inflammation in FVIIai treated mice with AIA was measured by external gamma counting of ^{99m}Tc uptake on days 1, 3, and 7 after antigen injection into the right (R) knee (a): Results are expressed as the ratio of ^{99m}Tc uptake in the right (R) arthritic knee joint to that in the left (L) uninflamed knee joint; for each time point the mean and SEM of the ratios are shown. On day 9 of AIA,

knee histologic features of control and FVIIai-treated mice were scored for synovial thickness (b), cartilage damage (c), and intraarticular fibrin deposition as evidenced by fibrin immunohistochemistry (d), using an arbitrary scale. Plasma was collected on day 9 of AIA from placebo treated and FVIIai treated mice, and the prothrombin time (PT) in seconds (sec) was determined (e). On day 9 of AIA fibrin deposition, as scored in (d), was associated with the PT in placebo treated and FVIIai treated mice (f). The horizontal bars represent the mean (e) or median (b-d). Statistical significance was tested by Wilcoxon's rank sum test and by fisher's exact test.

Please replace the last paragraph on page 38 of the specification with the following amended paragraph:

Figure 9 ~~Figure 7~~. Results of double staining wins anti TF and other antibodies on RA synovium (Staining was performed on synovial tissue specimens obtained from patients with rheumatoid arthritis (RA), using antibodies as described. Anti TF = anti tissue factor).

Please replace the third full paragraph on page 43 of the specification with the following amended paragraph:

Expression of TF, TFPI, and fibrin in RA Synovial membranes. Antibodies specific for TF, TFPI, and fibrin were used to stain sections of RA synovial membranes. Figure 1 shows a representative example of the distribution of the different antigens. TF staining was mainly perivascular and patchily distributed in interstitial layers. TF expression was demonstrated in fibroblasts, smooth muscle cells, and macrophages, but not in endothelial cells (Figure 1C). The latter observation was confirmed by double staining with cell specific markers; the results are summarized in Figure 9 ~~figure 7~~. TF immunohistochemistry was specific, because preadsorption of the TF antibody with an 8 x molar excess of

recombinant TF eliminated most of the staining (see Figure 1D). TFPI staining was observed on endothelial and subendothelial cells around blood vessels but was not found in all vessels. Fibrin was prominent in the synovial lining layer and in the deeper layers of the synovium. Fibrin was mainly associated with extracellular matrix but not with vascular or perivascular areas (Figures 1A and G). Fibrinogen staining was faint and evenly distributed throughout the synovial tissue, in contrast to the clearly localized staining seen with other antibodies (Figure 1F).